# WHY IS ANTIFUNGAL STEWARDSHIP IMPORTANT?

**Anna Khanina**

Antifungal Stewardship Project Manager – NCIC

PhD Candidate - NCIC

Clinical Pharmacist

NCIC NATIONAL CENTRE FOR INFECTIONS IN CANCER

# DISCLOSURES & CONFLICT OF INTEREST

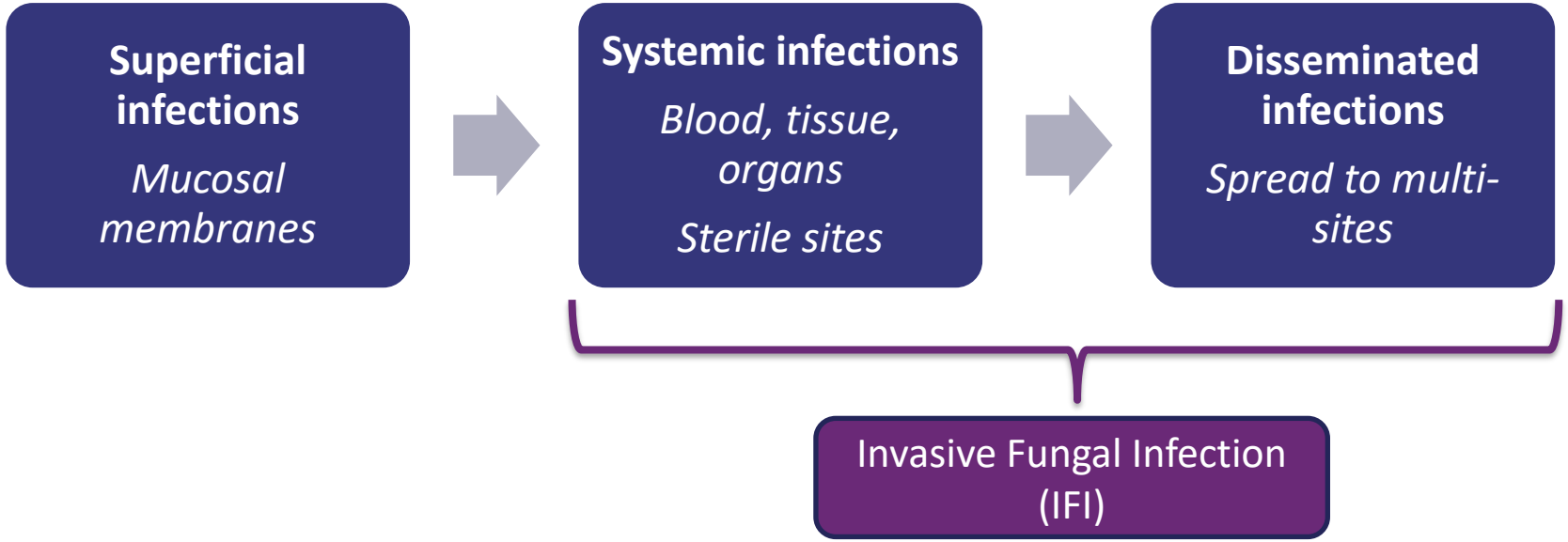
NIL DISCLOSURES

NIL CONFLICT OF INTEREST

# OVERVIEW

- What is invasive fungal infection?
- What is antifungal stewardship and why is it important?
- Reviewing antifungal stewardship in the literature
- Development of an evidence-based quality audit tool targeted at antifungal prescribing
- Overview of the Antifungal National Antimicrobial Prescribing Survey (AF-NAPS)

# INVASIVE FUNGAL INFECTION



# INVASIVE CANDIDA INFECTION

**Candidaemia**: Candida blood stream infection

**Deep tissue candidiasis:** Hepatosplenic candidiasis, endocarditis

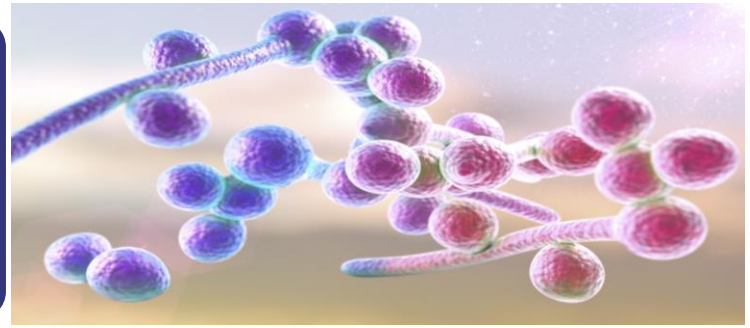
**Antifungal resistance**

*Candida albicans* most common → 0.9% fluconazole resistance[1]

↑ *Candida glabrata* (26.7%)[1] → Higher resistance to azoles

*Candida auris* → Multi-drug resistant

High Mortality ~ 40%[2]



**Risk factors** [3]

Intravascular catheters

TPN

Broad spectrum antibiotics

Immunosuppression

Diabetes

Acute renal failure

Haemodialysis

Prolonged ICU admission

Low birth weight

Premature babies in neonatal ICU


1. Chapman B et al. Journal of Antimicrobial Chemotherapy. 2017;72(4):1270-1270.
2. Pfaller M, *et al*. *Diagn Microbiol Infect Dis* 2012;74(4):323–331
3. Chen S, et al. Internal Medicine Journal. 2014;44(12b):1315-1332.

# INVASIVE MOULD INFECTION

**Invasive Aspergillosis**: Exposure to environmental spores via respiratory tract

Common sites of infection: Lungs & sinus most common

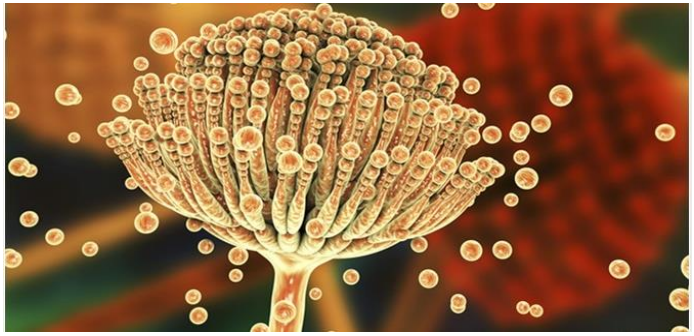
**Antifungal resistance**

Australia: < 3%[1]

Netherlands: 2004 1.7% triazole resistance → 2007 6% resistance

**High mortality**

30 – 80% depending on setting[3]



**Risk factors** [2]

Haematological malignancy

Stem cell transplant

Solid organ transplant

Severe prolonged neutropenia

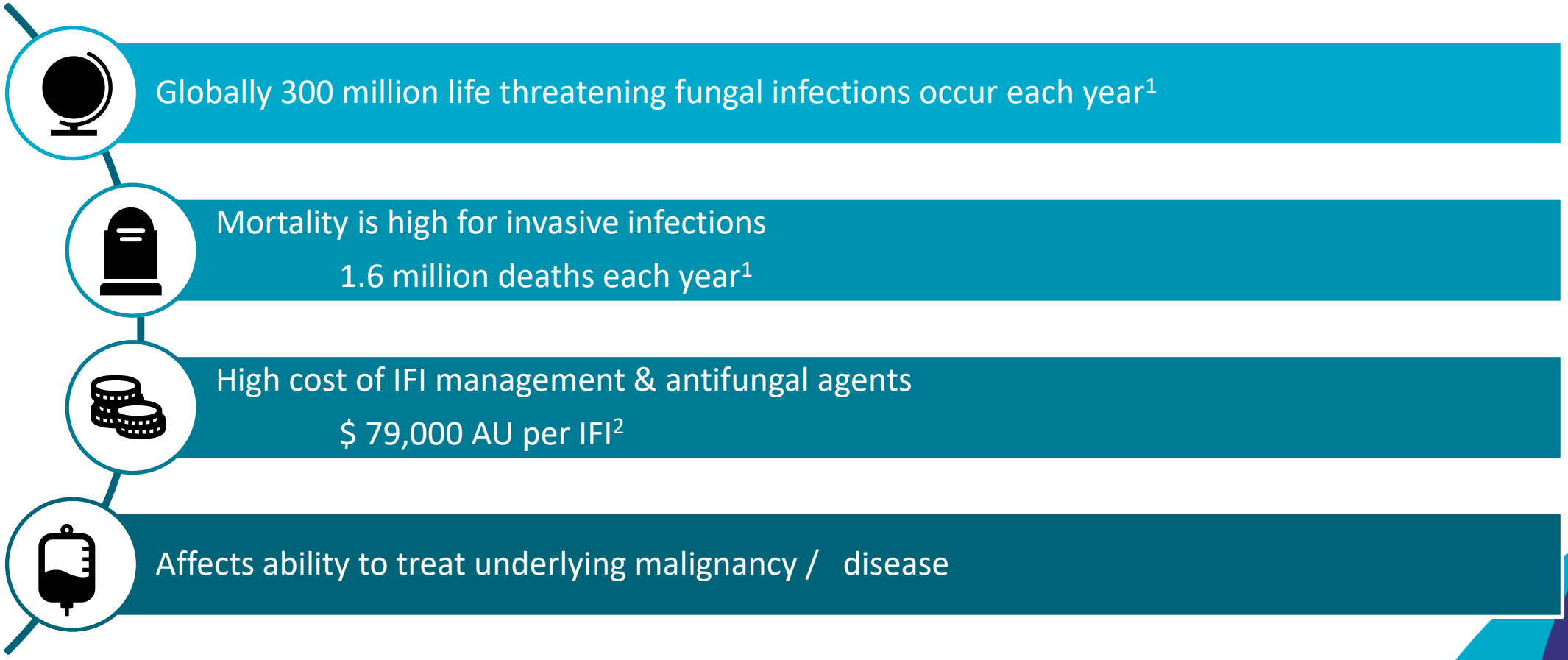
Corticosteroid use

**Non-*Aspergillus* mould infection**

- *Fusarium*, Lomentospora, *Sceodosporium*, Mucormycosis
- Limited antifungal options & difficult to treat
- Very high mortality rate


1. Kidd SE et al. Mycoses 2015; 58:350–5.
2. Fleming S et al. Internal Medicine Journal. 2014;44(12b):1283-1297.
3. Beardsley J, et al. Future Microbiology. 2018;13(10):1175-1191.

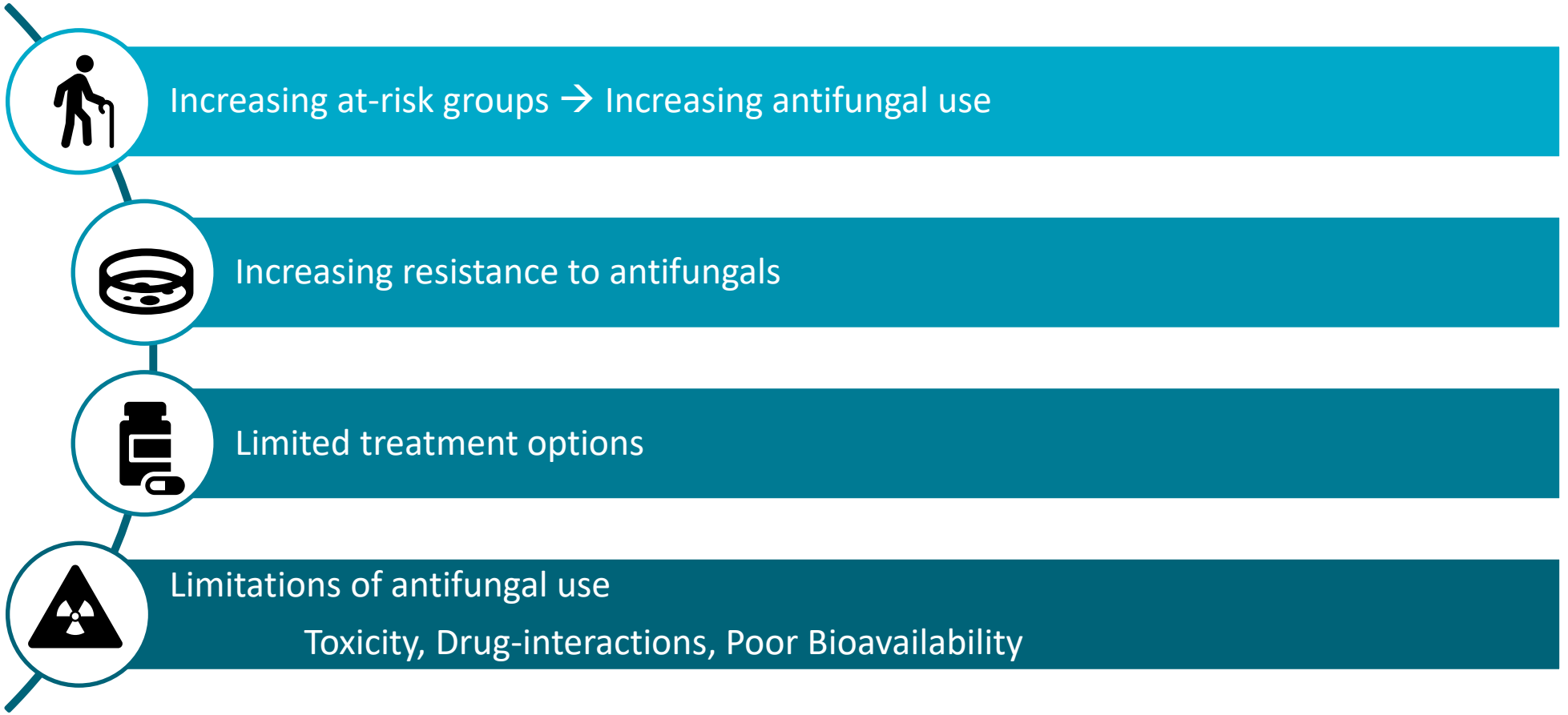
# FUNGAL INFECTION: WHY DO WE CARE?





1. Editorial. *Nat. Microbiol.* 2017;2(8):17120
2. Ananda-Rajah M et al. Antimicrobial Agents and Chemotherapy. 2011;55(5):1953-1960.

# FUNGAL INFECTION: WHY DO WE CARE?



# WHAT ARE THE GOALS OF ANTIFUNGAL STEWARDSHIP?


1. MacDougall C, et al. Clin Microbiol Rev 2005; 18:638–656.

# GUIDELINES FOR IMPLEMENTATION OF ANTIFUNGAL STEWARDSHIP

*The Journal of Infectious Diseases*

SUPPLEMENT ARTICLE

## Core Recommendations for Antifungal Stewardship: A Statement of the Mycoses Study Group Education and Research Consortium

Melissa D. Johnson,[1,a] Russell E. Lewis,[2,a] Elizabeth S. Dodds Ashley,[1,a] Luis Ostrosky-Zeichner,[3] Theoklis Zaoutis,[4] George R. Thompson III,[5] David R. Andes,[6] Thomas J. Walsh,[7] Peter G. Pappas,[8] Oliver Group Education and Research Consortium

INTERNAL MEDICINE JOURNAL

doi:10.1111/imj.15586

SUPPLEMENT ARTICLE

## Consensus guidelines for antifungal stewardship, surveillance and infection prevention, 2021

Anna Khanina,[1,2] Shio Yen Tio,[1,2] Michelle R. Ananda-Rajah,[3,4] Sarah E. Kidd,[5,6] Eloise Williams,[7,8] Lynette Chee,[9,10] Karen Urbancic[1,10,11,12] and Karin A. Thursky,[1,10,12,13,14] Australasian Antifungal Guidelines Steering Committee

# WHO SHOULD BE MEMBERS OF THE AFS TEAM?


- Build strong relationships and embed infectious diseases team member within high prescribing units (ideally!)
- Influence day to day decision making on IFI management & antifungal prescribing

AFS activities may be undertaken by existing AMS team with input from specialists in the area

Agrawal et al JAC 2016;71(2):37-42

# WHAT INTERVENTIONS EXIST FOR AFS?

## 1 Antifungal guidelines

INTERNAL MEDICINE JOURNAL
RACP Specialists. Together

doi:10.1111/imj.15585

SUPPLEMENT ARTICLE

**Introduction to the updated Australasian consensus guidelines for the management of invasive fungal disease and use of antifungal agents in the haematology/oncology setting, 2021**

Christina C. Chang,[1,2,3] Christopher C. Blyth,[4,5,6,7] Sharon C-A. Chen,[8,9,10] Anna Khanina,[11,12] C. Orla Morrissey,[13,14] Jason A. Roberts,[15,16,17] Karin A. Thursky,[11,18,19,20,21] Leon J. Worth[11,20] and Monica A. Slavin,[11,12,20,22] Australasian Antifungal Guidelines Steering Committee*

- C2: AFS & infection prevention
- C3: Optimising drug use & monitoring
- C4: Antifungal prophylaxis
- C5: Candida infections
- C6: Cryptococcus & rare yeasts
- C7: Invasive aspergillosis
- C8: Non aspergillus moulds
- C9: Patient information

**Adapt guidelines for local use**

Peter Mac

*Peter MacCallum Cancer Centre*
*Policies, Procedures and Guidelines*

**Guidelines for the antifungal prophylaxis in haematological malignancy and haemopoietic stem cell transplantation**

# WHAT INTERVENTIONS EXIST FOR AFS?

**Pre prescription approval**

Formulary restrictions but ensure timely access

**Post prescription review**

Perform at key optimisation time points

Timely discussion with clinical team to optimise therapy

**Fungal diagnostic & Therapeutic Drug Monitoring (TDM) stewardship**

Non -culture based tests, Imaging (CT, PET)

**Education**

**Ongoing audit & feedback loop**

# WHAT IS THE ROLE OF INFECTION PREVENTION IN AFS?

## Quality processes

- HEPA and other filtration systems
- Manage highly immunosuppressed patients in a HEPA-filtered ward
- Targeted air sampling prior to commissioning new ward or air-handling systems
- Educate high-risk about infection prevention measures

## Building works

- Multi-disciplinary team for pre-emptive planning
- Risk assessment and review of mechanical air filtration
- Reduce patient's exposure to dust, stagnant water and damp areas
- Targeted air sampling
- Antifungal prophylaxis

## Outbreak management

- Active and targeted surveillance for IFD cases
- Thorough review of infection-control measures
- Genotypic analysis and molecular typing to facilitate investigation
- Store fungal isolates for future analysis

Khanina A, Tio SY, Ananda-Rajah MR, Kidd SE, Williams E, Chee L, Urbancic K, Thursky KA; Australasian Antifungal Guidelines Steering Committee. Consensus guidelines for antifungal stewardship, surveillance and infection prevention, 2021. Intern Med J. 2021 Nov;51 Suppl 7(Suppl 1):18-36

# LITERATURE: ANTIFUNGAL APPROPRIATENESS

## HAEMATOLOGY & ONCOLOGY SETTING

6 studies published

**Appropriateness of antifungal prescribing**

29.4% - 56.5%

(Outlier 95.7%)

**Areas for improvement**

* Prolonged duration empiric of therapy
* Prolonged duration of prophylactic therapy
* High rates of drug-drug interactions
* Inappropriate selection of antifungal agent
* Incorrect loading and maintenance dose
* Poor utilization of TDM


1. Lachenmayr SJ et al. Mycoses. 2018;61(7):464-71.
2. Paige E et al. Leuk Lymphoma. 2019;60(10):2373-83.
3. Briquet C et al. Eur J Clin Pharm. 2018;20(4):1-8..
4. Berking S et al. Mycoses. 2017;60(9):600-6.
5. de Souza MC et al. Int J Clin Pharm. 2016;38(6):1398-406.
6. Nivoix Y et al. J Antimicrob Chemother. 2012;67(10):2506-13

# LITERATURE: IMPACT OF AFS PROGRAMS

## HAEMATOLOGY & ONCOLOGY SETTING

Before – after quasi experimental studies
Variable interventions

**Improved quality of prescribing**

- Antifungal indication
- Drug selection
- Dosing
- Reduced clinically significant drug-drug interactions

**Reduced antifungal consumption**

- Reduction in antifungal consumption by 40%
- Reduction in duration of antifungal prescribing

High rate of AFS recommendation acceptance

Improvement in **prescriber knowledge** of antifungal prescribing and IFI management


1. Santiago-Garcia B et al. Pediatr Blood Cancer. 2020;67(4):e27963
2. Alfandari S et al. Med Mal Infect. 2014;44(4):154-8.
3. Lachenmayr SJ et al. Infection. 2019;47(4):603-10
4. Marzolini MA et al. J Haematol. 2016;172(2):285-7

# LITERATURE: IMPACT OF AFS PROGRAMS

## VARIOUS SETTINGS

*Tropical Medicine and Infectious Disease*

*Systematic Review*

### The Impact of Antifungal Stewardship on Clinical and Performance Measures: A Global Systematic Review

Fares Albahar [1,*], Hamza Alhamad [1], Mohammad Abu Assab [1], Rana Abu-Farha [2], Lina Alawi [3] and Sara Khaleel [4]

Systematic review

December 2023

41 studies: USA, UK, Europe. Asia

**Key findings**

- Variable interventions: PPR, authorisation, management bundles
- Lower mortality: 13 / 22 studies, (1 x statistically significant)
- Reduced antifungal consumption: 10 / 22 studies
- Reduced antifungal spending: 12/18 studies
- Variable metrics employed, difficult to aggregate or compare data
- **Guideline adherence and quality measures reported very infrequently**

# DATA TO DRIVE QUALITY IMPROVEMENT

**Core Recommendations for AFS**

**MSG-RC 2020**

"Facilities should evaluate the quality of antifungal prescribing on a systematic basis, and use data-driven strategies to further optimise AFS interventions"

"Antifungal stewardship programs should ideally assess patient-level outcomes where possible"

"All antifungal stewardship programs should have a mec
for direct data feedback to prescribers"

BUT HOW?

Johnson MD, Lewis RE, Dodds Ashley ES, *et al.* Core recommendations for Antifungal Stewardship: A Statement of the Mycoses Study Group Education and research consortium. *The Journal of Infectious Diseases* 2020;**222**. doi:10.1093/infdis/jiaa394

# DEVELOPMENT OF AN ANTIFUNGAL DEEP DIVE AUDIT TOOL

**Antifungal Stewardship Literature Review**

Existing quality metrics, audit tools and methodologies

↓

**Delphi Study of International Experts in AFS**

Determine important and feasible metrics to measure AFS activities

↓

**Co-Design of AF-NAPS tool**

Multi-disciplinary steering group to develop content and definitions

↓

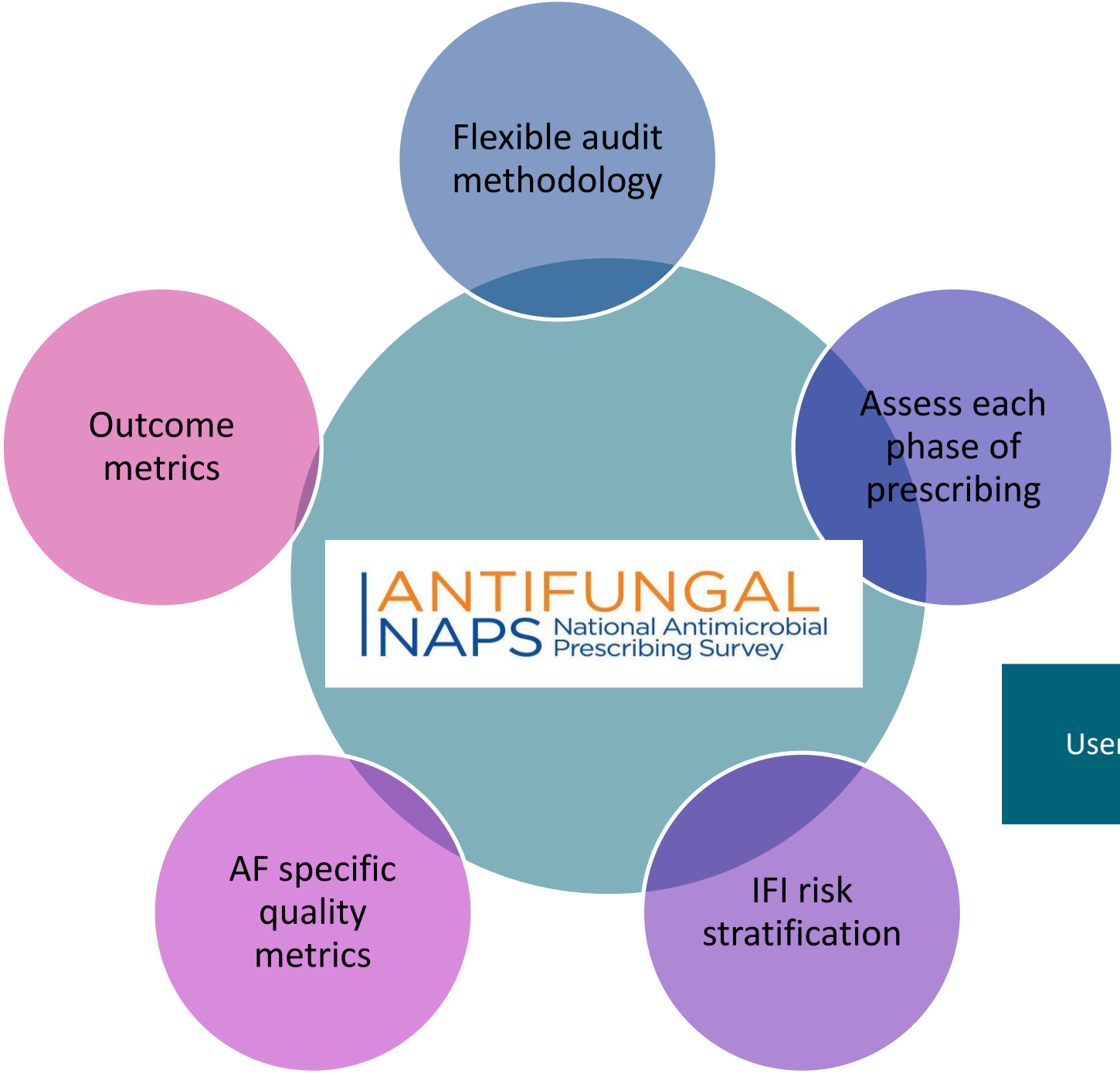
**Pilot use of AF-NAPS**

8 hospitals undertook pilot to test methodology, usability and provide feedback

↓

**Validation & Reliability study**

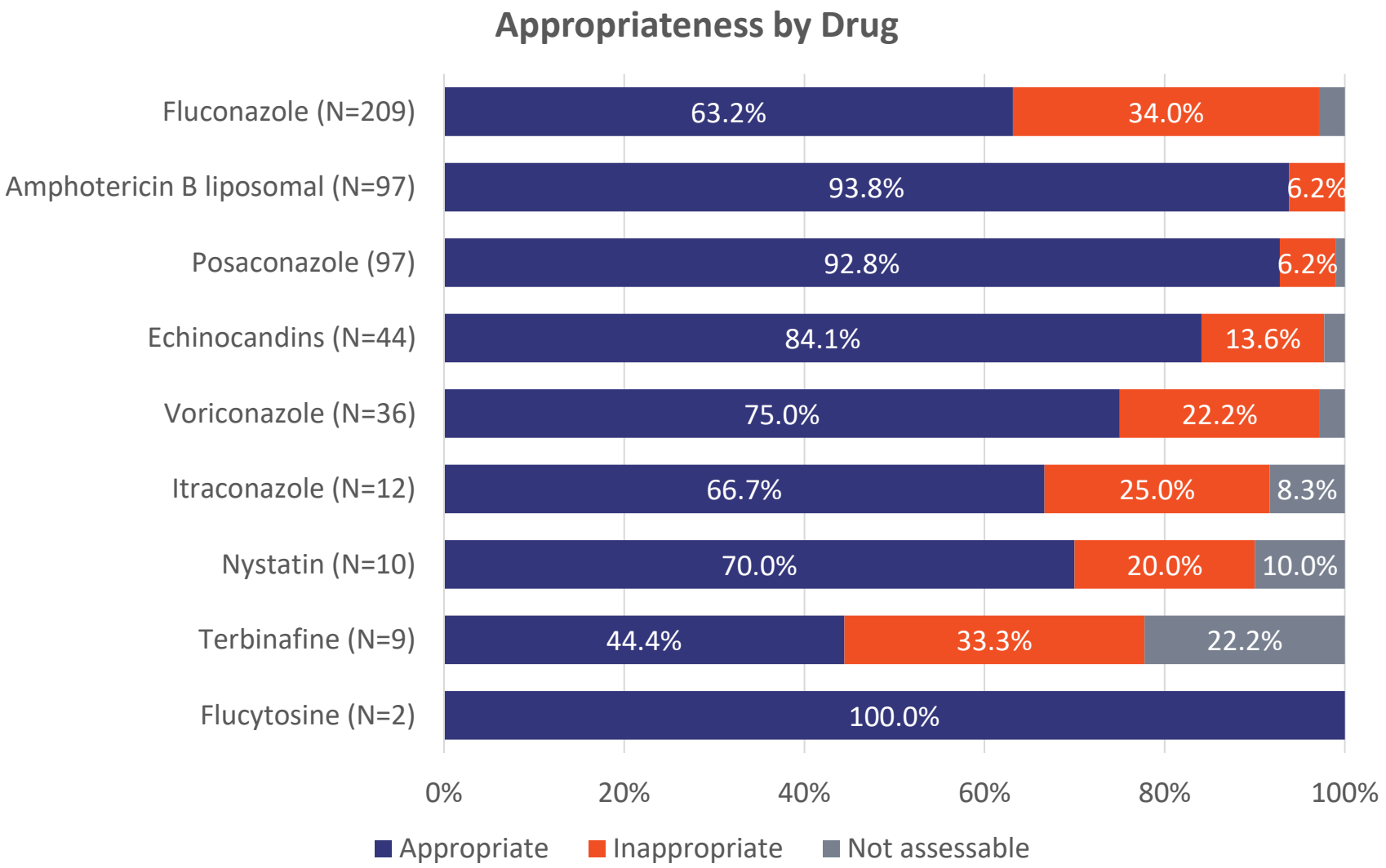
Aim to determine if the AF-NAPS tool is valid and reliable




## Antifungal NAPS resources

- User guide
- Appropriateness assessment matrix
- Instructional videos
- eLearning module
- Worked case examples

# ANTIFUNGAL NAPS 2023 RESULTS




11 Hospitals
438 Patients
516 Prescriptions

# ANTIFUNGAL NAPS 2023 RESULTS: FLUCONAZOLE

**Reasons for inappropriate empiric prescribing**

# SUMMARY

Antifungal Stewardship is essential to optimise the management of invasive fungal infection and improve patient outcomes for these serious infections

National & International guidelines are available to support implementation of stewardship & infection prevention measures

Literature on AFS show promising outcomes, however, require a greater focus on quality of antifungal prescribing and infection management

The Antifungal National Antimicrobial Prescribing Survey has been developed to support standardised deep dive audit of antifungal prescribing quality

# COLLABORATORS

PMCC ID

- Prof Karin Thursky
- Prof Monica Slavin
- Dr Abby Douglas
- A/Prof Gabrielle Haeusler
- Dr Ben Teh
- Dr Shio Yen Tio
- A/Prof Leon Worth
- Dr Olivia Smibert
- Dr Michelle Yong

PMCC Haem

- Dr Ashley Ng

NCIC

- Karen Urbancic
- A/Prof Lisa Hall
- Dr Daniel Yeoh

NCAS

- Dr Rodney James
- Robyn Ingram
- Xin Fang
- Dr Courtney Ierano
- Dr David Kong

Guidance

- Logesh Palani
- Abukari Yakubu

Pharmacists

- Emily Harding - RMH
- Cheryl Jackson - PMCC
- Janelle Penno- PMCC
- Miranda So – Canada
- Nikhil Singh - PMCC

NCIC NATIONAL CENTRE FOR INFECTIONS IN CANCER

# THANK YOU

Anna.Khanina@petermac.org

twitter @NCICancer

www.cancer**and**infections.org